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Barton, M

DOI: https://doi.org/10.1016/j.cardiores.2005.03.003

Originally published at:
Barton, M (2005). Aging and biomedicine 2005: Where should we go from here? Cardiovascular Research, 66(2):187-189.
DOI: https://doi.org/10.1016/j.cardiores.2005.03.003

ELSEVIER

Cardiovascular Research 66 (2005) 187–189

Cardiovascular Research

www.elsevier.com/locate/cardiores

Editorial

Aging and biomedicine 2005: Where should we go from here?

Matthias Barton*

Medizinische Poliklinik, Departement für Innere Medizin, Universitätsspital, Rämistrasse 100, CH-8091, Zürich, Switzerland

Received 28 February 2005; accepted 7 March 2005

1. Demographics of aging: the next 50 years

Aging has become a central issue in science and society in view of demographic changes anticipated in the next decades due to longevity and low birth rates [1–3]. The steady growth of the world's population from approximately 2.5 billion in 1950 to 6.4 billion today is expected to increase even further to more than 9 billion by 2050 [4] (Fig. 1). The reasons for living longer [5] involve a decline in old-age mortality [6] due to advances in disease management and drug discovery, which have been made possible through continued economic stability. However, despite these advances, today's clinical practice faces an increasing number of geriatric patients with multi-morbidity that requires special care adjusted to the high age of the patients.

2. Aging theories—all for one and one for all?

Age remains the main cause of death after age 28 in industrialized nations [7]. The majority of aging theories favors cumulative injury resulting in cellular senescence as a causative mechanism [8]. This results in genomic instability caused by DNA damage that varies between aging organ systems [9] and can be accelerated by reducing DNA repair capacity of the cell [10]. Since evidence also suggests that even within the same organ, aging may differently affect activity of proteins [11], aging is likely to exhibit distinct and specific rather than generalized responses, many of which are still not known. Concepts such as the "free radical theory of aging" proposed by Denham Harman in the 1950s [1,8] have suggested general mechanisms including oxidative stress to be predominantly responsible for cellular injury with aging. Evidence presented in recent years suggests that increased oxidative stress may indeed accelerate aging, at least in studies using short-lived species such as flies, nematodes, and laboratory animals [12].

Aging in humans, a "long-lived" species compared with those mentioned above, is far more complex than in other species, and, thus, knowledge obtained from non-human species should be applied with caution [13]. For example, human aging is associated with distinct metabolic changes such as impaired insulin sensitivity and altered steroid hormone function and lipid metabolism that require decades to develop. Aging also alters the body's responsiveness to dietary sodium and drugs and increases the activity of the sympathetic nervous system [8]. It is likely that these alterations contribute to some extent to the functional and structural changes found in aged human organ systems [14]. Moreover, after the fifth decade of life, a decrease in human skeletal muscle mass known as sarcopenia occurs [14], affecting approximately 25% of individuals aged 65 years and older and up to half of individuals above age 80 [14].

3. Cardiovascular aging: a point of no return?

The major cause of death worldwide currently continues to be cardiovascular disease, which affects aged men and women equally [15,16]. Given the anticipated growth of the aged population [5] (Fig. 1), the number of patients with cardiovascular risk factors and disease is expected to increase sharply, making early recognition, prevention, and treatment of risk factors and cardiovascular disease a pivotal issue [17]. Surprisingly, the aging cardiovascular system exhibits distinct changes that show a high degree of

* Tel.: +41 1 255 5663; fax: +41 1 255 8747.
E-mail address: barton@usz.ch.

doi:10.1016/j.cardiores.2005.03.003

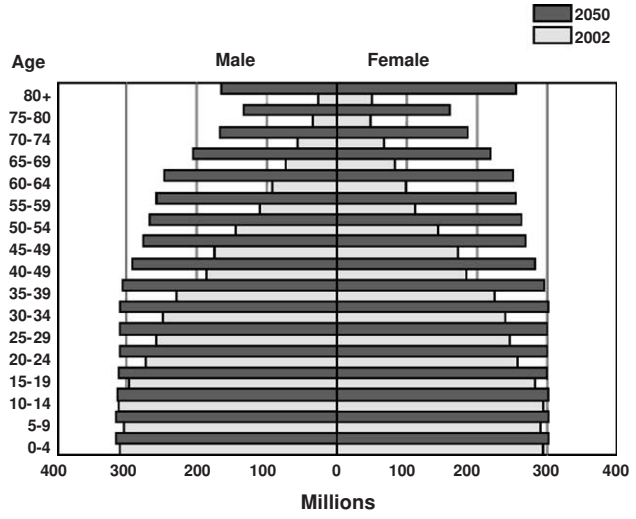

Fig. 1. Projected development of the world population. In addition to an expected growth of the world population from currently 6.2 billion to more than 9 billion in 2050, individuals aged 50 years and older will increase by a factor of 2 to 5 in both men and women, resulting in a pronounced shift in the overall population profile. Adapted from data provided by the U.S. Census Bureau, International Programs Center, International Data Base [5].

similarity between humans and rodents such as reduction in vascular and myocardial compliance as well as the development of vascular changes that can be modified by treatment [18].

Previously, aging has been viewed as "deteriorative changes with time during postmaturational life that underlie an increasing vulnerability to challenges, decreasing the ability of the organism to survive" [19]. This "deteriorative view" of aging resulting in gradual and irreversible loss of organ function has been recently challenged by intervention-induced improvement of age-related changes in the cardiovascular [20,21] and the central nervous system [22,23]. Surprisingly, certain neurological functions such as the ability to discriminate motion may actually improve with aging even in the absence of therapy [24], which indicates that there is need for more research on the physiology of aging.

4. Aging-associated "diseases": prevention rather than treatment

Much of the research on aging in recent years has been directed towards deciphering mechanisms and identifying targets that allow interference with the aging process and/or extension of life span. This Spotlight Issue of *Cardiovascular Research* features several viewpoints on important aspects of molecular, genetic, metabolic, and pathological changes related to cardiovascular aging written by experts in these fields. These articles not only summarize the current state of knowledge, but also illustrate the necessity to further and thoroughly investigate the mechanisms underlying the pathobiology of human aging.

Though solid scientific evidence is still lacking, the pharmaceutical and cosmetic industries over the years have devoted much activity to the economically rewarding field of aging "prevention".

Although there is a general desire for rejuvenation that is largely fueled by psychological and social factors, efforts should not be focused on finding "anti-aging" remedies. Rather, aging should be accepted as a physiologic process that does not require intervention but allows a high quality of life if the right steps are taken in due time.

What can we do to enable humans to "age gracefully" and to reduce the disease prevalence of many of the age-associated morbidities or to even prevent these morbidities that we are encountering in many of today's aged patients? These individuals frequently exhibit conditions favoring the development of hypertension, dyslipidemia, and atherosclerosis, including a high prevalence of obesity, lack of exercise, and unfavorable dietary regimens [17]. Unfortunately, these conditions are not limited to aged individuals but are already present to a considerable degree in juveniles [17,25]. It will thus require timely and powerful intervention if we want to avoid future disease in adulthood and even later in life.

Despite the availability of simple interventions such as improving cardiovascular fitness, a powerful tool to reduce cardiovascular mortality [26], improve plasticity in the aging human brain [23], and reduce immunosenescence [27] and even oxidative stress [28], or simply cutting down on food intake and maintaining a healthy body weight to delay aging-related changes [29–31], the potential of many of these measures is far from being fully recognized and is much underused. The goal of our efforts should not be to enable humans to live as long as possible but rather to have a life for as long as possible. Therefore, providing information to allow early prevention of disease will be the first step to successful aging.

Acknowledgements

I thank my colleagues for contributing to the original research reported here and the Schweizerische Nationalfonds, Bern (SNF Nr. 32.58421.99 SCORE and 32-58426.99/1), the Kurt und Senta Herrmann Stiftung, and the Hanne Liebermann Stiftung Zürich, Switzerland, for the support of my research.

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